

=> d his ful

FILE 'REGISTRY' ENTERED AT 12:41:40 ON 22 SEP 2003
 E NKG2D/CN
 E NKG 2D/CN

FILE 'HCAPLUS' ENTERED AT 12:42:17 ON 22 SEP 2003
 L1 515 SEA ABB=ON ?PROSTAT? (W) (?TUMOR? OR ?TUMOUR? OR ?CANCER? OR
 ?CARCIN? OR ?NEOPLASM?) (W) (?GROW? OR ?INCREAS? OR ?DEVEL?)
 L2 0 SEA ABB=ON L1 AND ?NKG2D?
 L3 1 SEA ABB=ON L1 AND ?RECEPTOR? (W) ?LIGAND?
 L4 D AU
 L4 1 SEA ABB=ON L1 AND NKG?
 L4 D AU
 L5 0 SEA ABB=ON L1 AND (MICA OR MICB OR ULBP)
 L6 2 SEA ABB=ON L1 AND (?NATURAL? (W) ?KILLER?)
 L7 0 SEA ABB=ON L1 AND ?CELL? (W) ?RECEPT?
 L8 165 SEA ABB=ON L1 AND ?RECEPT?
 L9 0 SEA ABB=ON L1 AND (MHC (W) ?CLASS? (W) (1 OR ONE))
 L10 0 SEA ABB=ON L1 AND (?RELATED? (W) ?CHAIN? (W) (A OR B))
 L11 0 SEA ABB=ON L1 AND UL (W) 16 (W) ?BIND? (W) ?PROTEIN?
 L12 4 SEA ABB=ON L3 OR L4 OR L6
 L13 4 SEA ABB=ON L12 OR L5 OR L7 OR L9 OR L10 OR L11 *4 hits from CA Plus*

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
 14:35:27 ON 22 SEP 2003
 L14 7 SEA ABB=ON L13
 L15 3 DUP REMOV L14 (4 DUPLICATES REMOVED) *3 hits from other db's*

* I included the "zero hits" items so they would ~~not~~ be
 searched in the "other db's."

Please let me know if you come up with add'l. ideas.

Thank you,
 M.J.
 605-1155

=> d que stat 113

```
L1      515 SEA FILE=HCAPLUS ABB=ON ?PROSTAT?(W) (?TUMOR? OR ?TUMOUR? OR
          ?CANCER? OR ?CARCIN? OR ?NEOPLASM?) (W) (?GROW? OR ?INCREAS? OR
          ?DEVEL?)
L3      1 SEA FILE=HCAPLUS ABB=ON L1 AND ?RECEPTOR?(W)?LIGAND?
L4      1 SEA FILE=HCAPLUS ABB=ON L1 AND NKG?
L5      0 SEA FILE=HCAPLUS ABB=ON L1 AND (MICA OR MICB OR ULBP)
L6      2 SEA FILE=HCAPLUS ABB=ON L1 AND (?NATURAL?(W)?KILLER?)
L7      0 SEA FILE=HCAPLUS ABB=ON L1 AND ?CELL?(W)?RECEPT?
L9      0 SEA FILE=HCAPLUS ABB=ON L1 AND (MHC(W)?CLASS?(W)(1 OR ONE))
L10     0 SEA FILE=HCAPLUS ABB=ON L1 AND (?RELATED?(W)?CHAIN?(W)(A OR
          B))
L11     0 SEA FILE=HCAPLUS ABB=ON L1 AND UL(W)16(W)?BIND?(W)?PROTEIN?
L12     4 SEA FILE=HCAPLUS ABB=ON L3 OR L4 OR L6
L13     4 SEA FILE=HCAPLUS ABB=ON L12 OR L5 OR L7 OR L9 OR L10 OR L11
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=> d 113 ibib abs 1-4

L13 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2003:511070 HCAPLUS
 DOCUMENT NUMBER: 139:64450
 TITLE: Prostate cancer diagnosis and outcome prediction by
 gene expression analysis
 INVENTOR(S): Golub, Todd R.; Febbo, Phillip G.; Ross, Kenneth N.;
 Sellers, William R.
 PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA;
 Dana-Farber Cancer Institute, Inc.
 SOURCE: PCT Int. Appl., 151 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053223	A2	20030703	WO 2002-US41209	20021220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003152980	A1	20030814	US 2002-325457	20021219
PRIORITY APPLN. INFO.:			US 2001-343448P	P 20011221

AB Methods identifying prostate cancer, methods for prognosing and diagnosing
 prostate cancer, methods for identifying a compd. that modulates
prostate cancer development, methods for detg.
 the efficacy of a prostate cancer therapy, and oligonucleotide microarrays
 contg. probes for genes involved in **prostate cancer development** are described. High-quality oligonucleotide-based
 expression data was obtained from 52 prostate tumors and 50 prostate
 samples lacking detectable tumor using Affymetrix human 95v microarrays
 contg. 12,600 total features for genes, ESTs, and controls. In

particular, a 5-gene model of prostate cancer outcome prediction is provided based on platelet-derived growth factor receptor .beta., chromogranin A, and HOXC6 (which show increased expression in recurrent tumors), while inositol triphosphate receptor type 3, and .beta.-galactoside sialotransferase show decreased expression in recurrent tumors.

L13 ANSWER 2 OF 4 HCPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:536130 HCPLUS
DOCUMENT NUMBER: 136:165765
TITLE: Inhibition of murine prostate tumor
growth and activation of immunoregulatory
cells with recombinant canarypox viruses
AUTHOR(S): Griffith, Thomas S.; Kawakita, Mutsushi; Tian, Jun;
Ritchey, Julie; Tartaglia, James; Sehgal, Inder;
Thompson, Timothy C.; Zhao, Weicheng; Ratliff, Timothy
L.
CORPORATE SOURCE: Department of Urology, University of Iowa, Iowa City,
IA, 52242-1089, USA
SOURCE: Journal of the National Cancer Institute (2001),
93(13), 998-1007
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Immunization with modified tumor cells carrying recombinant immunomodulatory genes is being explored as cancer immunotherapy. In this study, we examine whether canarypox ALVAC viruses carrying immunostimulatory cytokine genes (granulocyte-macrophage colony-stimulating factor, interleukin 2, interleukin 12, and tumor necrosis factor-.alpha.) can induce antitumor immunity (to rechallenge) in the RM-1 model of a highly aggressive, weakly immunogenic murine prostate cancer. Methods: For antitumor activity studies, RM-1 murine prostate cancer cells were infected with the parental ALVAC virus or one or two recombinant ALVAC-cytokine viruses and then injected into male C57BL/6 mice. For rechallenge studies, other mice were first given an injection s.c. with irradiated (nonproliferating) recombinant ALVAC-infected RM-1 cells and then (10 days later) with untreated RM-1 cells. For the detn. of which immune cells were required for antitumor activity, mice were immunodepleted of CD4, CD8, or natural killer (NK) NK1.1 cells with the corresponding monoclonal antibodies and were then given an injection of ALVAC-cytokine-infected RM-1 cells. For all expts., tumor outgrowth and animal survival were monitored. Results: After s.c. injection into mice, RM-1 cells infected with one (except ALVAC-interleukin 2) or two ALVAC-cytokine recombinants had statistically significantly greater antitumor activity than RM-1 cells infected with parental ALVAC ($P < .001$ for all; two-sided test). The antitumor activity of RM-1 cells infected with any two ALVAC-cytokine recombinants was greater than, but not statistically significantly different from, that of RM-1 cells infected with any one ALVAC-cytokine recombinant. NK1.1 cells were necessary for antitumor activity, but tumor-specific CD4+ regulatory T cells were also induced that inhibited CD8+ RM-1-specific cytotoxic T cells, resulting in the lack of immunity to a rechallenge by RM-1 cells. Discussion: Canarypox viruses can transfer immunostimulatory cytokine genes into RM-1 prostate cancer cells. When such cells were injected into mice, the cytokines induced an antitumor response against this highly aggressive, weakly immunogenic tumor. This response, however, did not protect the mouse against a rechallenge with RM-1 cells because suppressor CD4+ T cells were induced that inhibited tumor-specific CD8+ cytotoxic T cells.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2000:538306 HCAPLUS
 DOCUMENT NUMBER: 134:27966
 TITLE: Ligand-independent activation of the androgen receptor in prostate cancer by growth factors and cytokines
 AUTHOR(S): Jenster, Guido
 CORPORATE SOURCE: Department of Urology, Erasmus University Rotterdam, Rotterdam, 3000 DR, Neth.
 SOURCE: Journal of Pathology (2000), 191(3), 227-228
 CODEN: JPTLAS; ISSN: 0022-3417
 PUBLISHER: John Wiley & Sons Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review, with 27 refs. During the course of prostate cancer progression, cells convert from an androgen-dependent to an androgen-independent growth status. At this late stage, the role of the androgens testosterone and dihydrotestosterone and their nuclear receptor, the androgen receptor (AR), is unclear. Has the growth pathway, initiated by the AR, been bypassed in androgen-independent tumors? Mounting evidence suggests the opposite. Prostate cancer cells that have acquired the ability to survive and grow in a low-androgen environment might be activating the AR pathway using growth factors, cytokines, and steroids other than androgens.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1990:48424 HCAPLUS
 DOCUMENT NUMBER: 112:48424
 TITLE: Effects of the immunomodulator PSK on growth of human prostate adenocarcinoma in immunodeficient mice
 AUTHOR(S): Mickey, Don D.; Bencuya, Paul S.; Foulkes, Kathleen
 CORPORATE SOURCE: Dep. Surgery, Univ. North Carolina, Chapel Hill, NC, USA
 SOURCE: International Journal of Immunopharmacology (1989), 11(7), 829-38
 CODEN: IJIMDS; ISSN: 0192-0561
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Tumor growth alterations were studied using an immunomodulator, PSK. Four human prostate tumor lines were grown in two types of immunodeficient mice. Two of the lines were selected because they are able to metastasize to lungs in host animals. Outbred NIH Swiss athymic mice having normal natural killer cells and athymic Beige mice deficient in natural killer cells were used as animal hosts. PSK treatment was given to tumor-bearing hosts to some animals soon after solid tumors were injected and to others after solid tumors were well-established. Low dose cyclophosphamide was given to some animals to decrease host natural killer cells and poly I:C to other animals to increase natural killer cell activity. Measurement of tumor doubling times, host survival and metastatic capabilities showed that either poly I:C or PSK treatment in NIH Swiss animals soon after tumor cells were injected increased tumor doubling times and host survival and decreased the incidence and no. of metastatic lung lesions. Two of the tumor lines incapable of metastasizing in NIH Swiss mice were metastatic in the Beige athymic, natural killer-cell-deficient animals.

Harris 09/871,491

22/09/2003

=> d que stat 115

L1 515 SEA FILE=HCAPLUS ABB=ON ?PROSTAT?(W) (?TUMOR? OR ?TUMOUR? OR
?CANCER? OR ?CARCIN? OR ?NEOPLASM?) (W) (?GROW? OR ?INCREAS? OR
?DEVEL?)

L3 1 SEA FILE=HCAPLUS ABB=ON L1 AND ?RECEPTOR?(W) ?LIGAND?

L4 1 SEA FILE=HCAPLUS ABB=ON L1 AND NKG?

L5 0 SEA FILE=HCAPLUS ABB=ON L1 AND (MICA OR MICB OR ULBP)

L6 2 SEA FILE=HCAPLUS ABB=ON L1 AND (?NATURAL?(W) ?KILLER?)

L7 0 SEA FILE=HCAPLUS ABB=ON L1 AND ?CELL?(W) ?RECEPT?

L9 0 SEA FILE=HCAPLUS ABB=ON L1 AND (MHC(W) ?CLASS?(W) (1 OR ONE))

L10 0 SEA FILE=HCAPLUS ABB=ON L1 AND (?RELATED?(W) ?CHAIN?(W) (A OR
B))

L11 0 SEA FILE=HCAPLUS ABB=ON L1 AND UL(W)16(W)?BIND?(W) ?PROTEIN?

L12 4 SEA FILE=HCAPLUS ABB=ON L3 OR L4 OR L6

L13 4 SEA FILE=HCAPLUS ABB=ON L12 OR L5 OR L7 OR L9 OR L10 OR L11

L14 7 SEA L13

L15 3 DUP REMOV L14 (4 DUPLICATES REMOVED)

=> d 115 ibib abs 1-3

L15 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2001384796 MEDLINE

DOCUMENT NUMBER: 21331884 PubMed ID: 11438565

TITLE: Inhibition of murine prostate tumor
growth and activation of immunoregulatory cells
with recombinant canarypox viruses.

AUTHOR: Griffith T S; Kawakita M; Tian J; Ritche J; Tartaglia J;
Sehgal I; Thompson T C; Zhao W; Ratliff T L

CORPORATE SOURCE: Department of Urology, University of Iowa, Iowa City
52242-1089, USA.. thomas-griffith@uiowa.edu

CONTRACT NUMBER: 1R01CA89062-01 (NCI)

SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE, (2001 Jul 4) 93
(13) 998-1007.
Journal code: 7503089. ISSN: 0027-8874.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200107

ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726

AB BACKGROUND: Immunization with modified tumor cells carrying recombinant immunomodulatory genes is being explored as cancer immunotherapy. In this study, we examine whether canarypox ALVAC viruses carrying immunostimulatory cytokine genes (granulocyte-macrophage colony-stimulating factor, interleukin 2, interleukin 12, and tumor necrosis factor-alpha) can induce antitumor immunity (to rechallenge) in the RM-1 model of a highly aggressive, weakly immunogenic murine prostate cancer. METHODS: For antitumor activity studies, RM-1 murine prostate cancer cells were infected with the parental ALVAC virus or one or two recombinant ALVAC-cytokine viruses and then injected into male C57BL/6 mice. For rechallenge studies, other mice were first given an injection subcutaneously with irradiated (nonproliferating) recombinant ALVAC-infected RM-1 cells and then (10 days later) with untreated RM-1 cells. For the determination of which immune cells were required for antitumor activity, mice were immunodepleted of CD4, CD8, or natural killer (NK) NK1.1 cells with the corresponding

monoclonal antibodies and were then given an injection of ALVAC-cytokine-infected RM-1 cells. For all experiments, tumor outgrowth and animal survival were monitored. RESULTS: After subcutaneous injection into mice, RM-1 cells infected with one (except ALVAC-interleukin 2) or two ALVAC-cytokine recombinants had statistically significantly greater antitumor activity than RM-1 cells infected with parental ALVAC ($P<.001$ for all; two-sided test). The antitumor activity of RM-1 cells infected with any two ALVAC-cytokine recombinants was greater than, but not statistically significantly different from, that of RM-1 cells infected with any one ALVAC-cytokine recombinant. NK1.1 cells were necessary for antitumor activity, but tumor-specific CD4(+) regulatory T cells were also induced that inhibited CD8(+) RM-1-specific cytotoxic T cells, resulting in the lack of immunity to a rechallenge by RM-1 cells. DISCUSSION: Canarypox viruses can transfer immunostimulatory cytokine genes into RM-1 prostate cancer cells. When such cells were injected into mice, the cytokines induced an antitumor response against this highly aggressive, weakly immunogenic tumor. This response, however, did not protect the mouse against a rechallenge with RM-1 cells because suppressor CD4(+) T cells were induced that inhibited tumor-specific CD8(+) cytotoxic T cells.

L15 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 ACCESSION NUMBER: 1999:184908 BIOSIS
 DOCUMENT NUMBER: PREV199900184908
 TITLE: Disruption of the polyglutamine tract results in increased ligand-induced transcriptional activity of the androgen receptor.
 AUTHOR(S): Yang, M.; Raynor, M.; Neufing, P. J.; Buchanan, G.; Tilley, W. D.
 CORPORATE SOURCE: Flinders Cancer Cent., Flinders Univ. South Aust., Flinders Med. Cent., Adelaide, SA 5042 Australia
 SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 408.
 Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
 ISSN: 0197-016X.
 DOCUMENT TYPE: Conference
 LANGUAGE: English

L15 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 88192256 MEDLINE
 DOCUMENT NUMBER: 88192256 PubMed ID: 3128959
 TITLE: Leuproreotide vs. diethylstilboestrol: effect on natural killer cells.
 AUTHOR: Ablin R J; Gonder M J; Bartkus J M
 CORPORATE SOURCE: Department of Urology, State University of New York, Stony Brook 11794.
 CONTRACT NUMBER: RR05736 (NCRR)
 SOURCE: ANTICANCER RESEARCH, (1988 Jan-Feb) 8 (1) 73-6.
 Journal code: 8102988. ISSN: 0250-7005.
 PUB. COUNTRY: Greece
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198805
 ENTRY DATE: Entered STN: 19900308
 Last Updated on STN: 19970203
 Entered Medline: 19880516
 AB Recent studies suggest even low dosages of oestrogen currently used for

treatment of prostate cancer increase cardiovascular morbidity. In addition, relapse following growth of hormone - insensitive cells, and the present observations of further evidence of immunosuppression demonstrated by the significant (p less than 0.001) effect of DES on the lytic activity of **natural killer** cells vs. the negligible effect of the luteinizing - hormone - releasing - hormone, leuprolide (Lupron) raises concern that the palliative effects of oestrogen therapy are possibly further compromised by a reduction in immunosurveillance to tumour, or equally important, by a decreased capacity to cope with infectious agents.

Inventor Search

Harris 09/871,491

22/09/2003

=> d_ibib_abs.ind 118 1-11

L18 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:137769 HCAPLUS
DOCUMENT NUMBER: 138:203620
TITLE: A novel ligand for the NKG2D receptor activates NK cells and macrophages and induces tumor immunity
AUTHOR(S): Diefenbach, Andreas; Hsia, Jennifer K.; Hsiung, Ming-Yu B.; Raulet, David H.
CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer Research Laboratory, University of California, Berkeley, USA
SOURCE: European Journal of Immunology (2003), 33(2), 381-391
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB NK cells are involved in the immune response against viral and microbial infections and tumors. In contrast to B and T cells, NK cells employ various modes of immune recognition. An important mode of immune recognition employed by NK cells is "induced self recognition" exemplified by the NKG2D receptor-ligand system. The NKG2D immunoreceptor, expressed by NK cells, and by activated CD8+ T cells and macrophages, recognizes one of several cell surface ligands that are distantly related to MHC class I mols. (i.e. H60 and Rael proteins in mice, and MHC class I chain-related proteins and UL-16-binding proteins in humans). These ligands are not expressed abundantly by most normal cells but are up-regulated on cells exposed to various forms of cellular insults. Here the authors report the cloning of another ligand for NKG2D; transcripts of this ligand are found in a wide variety of tissues and in various tumor cells. Crosslinking of NKG2D with the novel ligand potently activated NK cells and macrophages. Tumor cells ectopically expressing the mol. were efficiently rejected by naive mice, and induced strong protective immunity to the parental, ligand-neq. tumor cells.

CC 15-10 (Immunochemistry)

ST ligand NKG2D receptor NK cell macrophage tumor immunity

IT Lymphoma

(B-cell; novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity)

IT Ligands

RL: BSU (Biological study, unclassified); BIOL (Biological study) (MULT1 ligand, of NKG2D receptor MULT1; novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity)

IT Lymphoma

(T-cell; novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity)

IT Prostate gland, neoplasm

(carcinoma; novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity)

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene NKG2D; novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity)

IT Lymphocyte

(natural killer cell; novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity)

IT Mast cell ($n = 30$)

(neoplasm, mastocytoma; novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity) tumor agents.

IT Antitumor agents

Human

Macrophage

Spleen

Thyme (Thymus)

(novel ligand for NKG2D receptor activates NK cells and macrophages and induces tumor immunity)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:967899 HCAPLUS

DOCUMENT NUMBER: 138:151737

TITLE: The innate immune response to tumors and its role in the induction of T-cell immunity

AUTHOR(S): Diefenbach, Andreas; Raulet, David H.

CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer Research Laboratory, University of California, Berkeley, CA, USA

SOURCE: Immunological Reviews (2002), 188, 9-21
CODEN: IMRED2; ISSN: 0105-2896

PUBLISHER: Blackwell Munksgaard

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Recent genetic studies have resurrected the concept that the adaptive and innate immune systems play roles in tumor surveillance. Natural killer (NK) cells recognize many tumor cells but not normal self cells, and they are thought to aid in the elimination of nascent tumors. Two main strategies are employed by NK cells to recognize tumor targets. Many tumor cells down-regulate class I major histocompatibility complex (MHC) mols., thus releasing the NK cell from the inhibition provided by class I MHC-specific inhibitory receptors ('missing self recognition'). More recently, it has become clear that a stimulatory receptor expressed by NK cells, T cells and macrophages (NKG2D) recognizes ligands (MHC class I chain related [MIC], H60, retinoic acid early inducible [Raell] and UL16 binding proteins [ULBP]) that are up-regulated on tumor cells and virally infected cells but are not expressed well by normal cells. Ectopic expression of these ligands on tumor cells leads to the potent rejection of the tumors *in vivo*. Importantly, mice that previously rejected the ligand+ tumor cells develop T-cell immunity to the parental (ligand-) tumor cells. The recognition of induced-self ligands as a strategy to recognize abnormal self sets a precedent for a new immune recognition strategy of the innate immune system.

CC 15-0 (Immunochemistry)

ST review tumor recognition natural killer cell NKG2D receptor

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC class I chain related protein; innate immune response to tumors and its role in the induction of T-cell immunity and recognition of)

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NKG2D; innate immune response to tumors and its role in the induction of T-cell immunity)

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(UL16; innate immune response to tumors and its role in the induction of T-cell immunity and recognition of)

IT Immunity

(immune surveillance; innate immune response to tumors and its role in the induction of T-cell immunity)

IT Human
 T cell (lymphocyte)
 (innate immune response to tumors and its role in the induction of
 T-cell immunity)

IT Proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (retinoic acid early inducible protein; innate immune response to
 tumors and its role in the induction of T-cell immunity and recognition
 of)

REFERENCE COUNT: 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L18 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:953327 HCAPLUS
 DOCUMENT NUMBER: 138:105220
 TITLE: Innate immune recognition by stimulatory
 immunoreceptors
 AUTHOR(S): Diefenbach, Andreas; Raulet, David
 H.
 CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer
 Research Laboratory, University of California,
 Berkeley, CA, 94720, USA
 SOURCE: Current Opinion in Immunology (2003), 15(1), 37-44
 CODEN: COPIEL; ISSN: 0952-7915
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. The specificity of cells of the innate immune system is detd. in part by various stimulatory receptors that function in different forms of immune recognition. NKG2D, a stimulatory receptor expressed by natural killer (NK) cells, macrophages and certain T cell subsets, recognizes various families of induced-self' ligands. The ligands are distantly related to class I MHC mols. and are induced in distressed' cells as markers of abnormal self. Another form of innate immune recognition is exemplified by the Ly49H receptor, which is expressed by a subset of NK cells. The Ly49H receptor directly recognizes a virus-encoded protein expressed by cells infected with mouse cytomegalovirus (MCMV) and the Ly49h gene is identical to the Cmv1R gene, which confers resistance to MCMV infections. Yet another group of receptors (the triggering receptors expressed by myeloid cells, or TREMs), which are exclusively expressed by myeloid cells, have been shown to amplify cytokine responses to bacterial products and have also been implicated in the pathogenesis of septic shock.

CC 15-0 (Immunochemistry)
 ST review innate immunity antigen recognition immunostimulation
 immunoreceptors
 IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (Ly49H; innate immune recognition by stimulatory immunoreceptors)
 IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (NKG2D; innate immune recognition by stimulatory immunoreceptors)
 IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (TREM (the triggering receptors expressed by myeloid cells); innate
 immune recognition by stimulatory immunoreceptors)
 IT Immunostimulation
 (innate immune recognition by stimulatory immunoreceptors)
 IT Immunity

(innate; innate immune recognition by stimulatory immunoreceptors)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:927272 HCAPLUS
 DOCUMENT NUMBER: 137:383795
 TITLE: Tumor therapy
 INVENTOR(S): Raulet, David H.; Diefenbach, Andreas
 PATENT ASSIGNEE(S): The Regents of the University of California, USA
 SOURCE: PCT Int. Appl., 32 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096459	A1	20021205	WO 2002-US16924	20020531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
US 2002187151	A1	20021212	US 2001-871491	20010531

PRIORITY APPLN. INFO.: US 2001-871491 A 20010531

AB Neoplasia is treated by administering to a mammalian host a compn. comprising ligands for the NKG2D receptor. In addn., other NKG2D ligands, proteins specific for the neoplastic cells and cytokines may be included to enhance the immune response. The compn. may be cells comprising expression constructs for the ligands, liposomes or combinations of proteins mols.

IC ICM A61K039-395
 ICS A61K031-00; A61K038-00; G01N033-48; A01N061-00; C07K001-00; C07K002-00; C07K004-00; C07K005-00; C07K007-00; C07K014-00; C07K016-00; C07K017-00

CC 15-2 (Immunochemistry)

Section cross-reference(s): 1, 63

ST NKG2D receptor ligand antitumor therapy

IT Histocompatibility antigens

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (MHC (major histocompatibility complex), class I; tumor therapy with NKG2D receptor ligands)

IT Antigen-presenting cell

(MICA, MICB, and ULBP; tumor therapy with NKG2D receptor ligands)

IT Receptors

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NKG2D, ligands for; tumor therapy with NKG2D receptor ligands)

IT Antibodies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NKG2D-specific; tumor therapy with NKG2D receptor ligands)

IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (lectin, lectin-like NKG2D receptor; tumor therapy with NKG2D receptor ligands)

IT Drug delivery systems
 (liposomes; tumor therapy with NKG2D receptor ligands)

IT Neoplasm
 (metastasis; tumor therapy with NKG2D receptor ligands)

IT T cell (lymphocyte)
 (natural killer; tumor therapy with NKG2D receptor ligands)

IT Antitumor agents
 Neoplasm
 (tumor therapy with NKG2D receptor ligands)

IT Cytokines
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (tumor therapy with NKG2D receptor ligands)

IT Proteins
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tumor therapy with NKG2D receptor ligands)

IT Ligands
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (tumor therapy with NKG2D receptor ligands)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 11 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:894238 HCPLUS
 DOCUMENT NUMBER: 138:54480
 TITLE: Selective associations with signaling proteins determine stimulatory versus costimulatory activity of NKG2D
 AUTHOR(S): Diefenbach, Andreas; Tomasello, Elena;
 Lucas, Matthias; Jamieson, Amanda M.; Hsia, Jennifer K.; Vivier, Eric; Raulet, David H.
 CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer Research Laboratory, University of California, Berkeley, CA, 94720-3200, USA
 SOURCE: Nature Immunology (2002), 3(12), 1142-1149
 CODEN: NIAMCZ; ISSN: 1529-2908
 PUBLISHER: Nature Publishing Group
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Optimal lymphocyte activation requires the simultaneous engagement of stimulatory and costimulatory receptors. Stimulatory immunoreceptors are usually composed of a ligand-binding transmembrane protein and noncovalently assocd. signal-transducing subunits. Here, we report that alternative splicing leads to two distinct NKG2D polypeptides that assoc. differentially with the DAP10 and KARAP (also known as DAP12) signaling subunits. We found that differential expression of these isoforms and of signaling proteins detd. whether NKG2D functioned as a costimulatory receptor in the adaptive immune system (CD8+ T cells) or as both a primary recognition structure and a costimulatory receptor in the innate immune system (natural killer cells and macrophages). This strategy suggests a rationale for the multisubunit structure of stimulatory immunoreceptors.
 CC 15-10 (Immunochemistry)
 ST signaling protein DAP10 KARAP stimulation
 IT Proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

(DAP10; selective assocns. with signaling proteins det. stimulatory vs. costimulatory activity of NKG2D)

IT Proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (DAP12; selective assocns. with signaling proteins det. stimulatory vs. costimulatory activity of NKG2D)

IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (NKG2D, splice variants; selective assocns. with signaling proteins det. stimulatory vs. costimulatory activity of NKG2D)

IT Lymphocyte
 (natural killer cell; selective assocns. with signaling proteins det. stimulatory vs. costimulatory activity of NKG2D on)

IT Signal transduction, biological
 (selective assocns. with signaling proteins det. stimulatory vs. costimulatory activity of NKG2D)

IT CD8-positive T cell
 Macrophage
 (selective assocns. with signaling proteins det. stimulatory vs. costimulatory activity of NKG2D on)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:878952 HCAPLUS

DOCUMENT NUMBER: 137:351328

TITLE: Tumor rejection mediated by NKG2D receptor-ligand interaction is dependent upon perforin

AUTHOR(S): Hayakawa, Yoshihiro; Kelly, Janice M.; Westwood, Jennifer A.; Darcy, Phillip K.; Diefenbach, Andreas; Raulet, David; Smyth, Mark J.

CORPORATE SOURCE: Cancer Immunology Program, Sir Donald and Lady Trescowthick Laboratories, Peter MacCallum Cancer Institute, East Melbourne, 8006, Australia

SOURCE: Journal of Immunology (2002), 169(10), 5377-5381
 CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have investigated the primary immunity generated in vivo by MHC class I-deficient and -competent tumor cell lines that expressed the NKG2D ligand retinoic acid early inducible-1 (Rae-1).beta.. Rae-1.beta. expression on class I-deficient RMA-S lymphoma cells enhanced primary NK cell-mediated tumor rejection in vivo, whereas RMA-Rae-1.beta. tumor cells were rejected by a combination of NK cells and CD8+ T cells. Rae-1.beta. expression stimulated NK cell cytotoxicity and IFN-.gamma. secretion in vitro, but not proliferation. Surprisingly, only NK cell perforin-mediated cytotoxicity, but not prodn. of IFN-.gamma., was crit. for the rejection of Rae-1.beta.-expressing tumor cells in vivo. This distinct requirement for perforin activity contrasts with the NK cell-mediated rejection of MHC class I-deficient RMA-S tumor cells expressing other activating ligands such as CD70 and CD80. Thus, these results indicated that NKG2D acted as a natural cytotoxicity receptor to stimulate perforin-mediated elimination of ligand-expressing tumor cells.

CC 15-8 (Immunochemistry)

ST tumor rejection NKG2D receptor ligand perforin

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (NKG2D; tumor rejection mediated by NKG2D receptor-ligand interaction is dependent upon perforin)

- IT Gene, animal
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (Rae-1; tumor rejection mediated by NKG2D receptor-ligand interaction
 is dependent upon perforin and)
- IT Lymphoma
 (T-cell, rejection; tumor rejection mediated by NKG2D receptor-ligand
 interaction is dependent upon perforin)
- IT Perforin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (tumor rejection mediated by NKG2D receptor-ligand interaction is
 dependent upon perforin)
- REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:603684 HCAPLUS
 DOCUMENT NUMBER: 138:302528
 TITLE: The role of the NKG2D immunoreceptor in immune cell
 activation and natural killing
 AUTHOR(S): Jamieson, Amanda M.; Diefenbach, Andreas;
 McMahon, Christopher W.; Xiong, Na; Carlyle, James R.;
 Raulet, David H.
 CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer
 Research Laboratory, University of California,
 Berkeley, CA, 94720, USA
 SOURCE: Immunity (2002), 17(1), 19-29
 CODEN: IUNIEH; ISSN: 1074-7613
 PUBLISHER: Cell Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Little is known concerning the stimulatory receptors responsible for tumor cell lysis by NK cells. The authors generated a monoclonal antibody specific for murine NKG2D to investigate its function. Blocking of NKG2D inhibited natural cytotoxicity of all tumor cells tested that express ligands for the receptor. Staining anal. showed that NKG2D is also expressed by activated CD8+ T cells and macrophages, and subsets of TCR.gamma..delta.+ and NK1.1+ T cells. Contradicting reports that NKG2D is solely a costimulatory receptor, the authors obsd. that crosslinking of NKG2D directly stimulates NK cells and activated macrophages. In contrast, NKG2D costimulates activated CD8+ T cells. Thus, NKG2D engagement directly stimulates NK cells and macrophages, costimulates CD8+ T cells, and plays a substantial role in natural killing.

- CC 15-10 (Immunochemistry)
 ST NKG2D immunoreceptor NK cell T lymphocyte macrophage activation
 IT T cell (lymphocyte)
 (NK1.1+; NKG2D immunoreceptor in immune cell activation and natural killing)
 IT CD8-positive T cell
 Cell activation
 Cytolysis
 Macrophage
 (NKG2D immunoreceptor in immune cell activation and natural killing)
 IT Tumor necrosis factors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (NKG2D immunoreceptor in immune cell activation and natural killing)
 IT T cell (lymphocyte)
 (TCR.gamma..delta.+; NKG2D immunoreceptor in immune cell activation and natural killing)
 IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

(gene NKG2D; NKG2D immunoreceptor in immune cell activation and natural killing)

IT Antibodies

RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (monoclonal, MI-6; NKG2D immunoreceptor in immune cell activation and natural killing)

IT Lymphocyte

(natural killer cell; NKG2D immunoreceptor in immune cell activation and natural killing)

IT Interferons

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (.gamma.; NKG2D immunoreceptor in immune cell activation and natural killing)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:707947 HCAPLUS

DOCUMENT NUMBER: 136:4572

TITLE: Rael and H60 ligands of the NKG2D receptor stimulate tumour immunity

AUTHOR(S): Diefenbach, Andreas; Jansen, Eric R.;
 Jamison, Amanda M.; Raulet, David H.

CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer Research Lab., University of California, Berkeley, 94720, USA

SOURCE: Nature (London, United Kingdom) (2001), 413(6852), 165-171

CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Natural killer (NK) cells attack many tumor cell lines, and are thought to have a crit. role in anti-tumor immunity; however, the interaction between NK cells and tumor targets is poorly understood. The stimulatory lectin-like NKG2D receptor is expressed by NK cells, activated CD8+ T cells and by activated macrophages in mice. Several distinct cell-surface ligands that are related to class I major histocompatibility complex mols. have been identified, some of which are expressed at high levels by tumor cells but not by normal cells in adults. However, no direct evidence links the expression of these 'induced self' ligands with tumor cell rejection. Here the authors demonstrate that ectopic expression of the murine NKG2D ligands Rael.beta. or H60 in several tumor cell lines results in potent rejection of the tumor cells by syngeneic mice. Rejection is mediated by NK cells and/or CD8+ T cells. The ligand-expressing tumor cells induce potent priming of cytotoxic T cells and sensitization of NK cells in vivo. Mice that are exposed to live or irradiated tumor cells expressing Rael or H60 are specifically immune to subsequent challenge with tumor cells that lack NKG2D ligands, suggesting application of the ligands in the design of tumor vaccines.

CC 15-8 (Immunochemistry)

ST Rael ligand NKG2D receptor tumor immunity; H60 ligand NKG2D receptor tumor immunity

IT Proteins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (H60; tumor rejection is induced by Rael and H60 ligands of NKG2D receptor)

IT Proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (NKG2D; tumor rejection is induced by Rael and H60 ligands of NKG2D receptor)

IT Proteins
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (Rael.beta.; tumor rejection is induced by Rael and H60 ligands of NKG2D receptor)

IT T cell (lymphocyte)
 (cytotoxic; tumor rejection is induced by Rael and H60 ligands of NKG2D receptor)

IT Lymphocyte
 (natural killer cell; tumor rejection is induced by Rael and H60 ligands of NKG2D receptor)

IT Neoplasm
 (tumor rejection is induced by Rael and H60 ligands of NKG2D receptor)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 11 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2001:659191 HCPLUS
 DOCUMENT NUMBER: 136:245871
 TITLE: Strategies for target cell recognition by natural killer cells
 AUTHOR(S): Diefenbach, Andreas; Raulet, David H.
 CORPORATE SOURCE: Department of Molecular & Cell Biology and Cancer Research Laboratory, University of California Berkeley, Berkeley, CA, 94720-3200, USA
 SOURCE: Immunological Reviews (2001), 181, 170-184
 CODEN: IMRED2; ISSN: 0105-2896
 PUBLISHER: Munksgaard International Publishers Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 AB A review. Stimulation of natural killer (NK) cells is regulated by a complex balance of inhibitory and stimulatory receptors expressed by NK cells. However, the interaction of stimulatory receptors and their ligands is poorly understood. One stimulatory receptor, NKG2D, is expressed by all NK cells, stimulated CD8+ T cells, .gamma..delta. T cells and macrophages. Recently, progress has been made in defining cellular ligands for NKG2D. Four different families of ligands have been identified in mice and humans, all of which are distantly related to MHC class I mols. Some of the ligands are upregulated in transformed and infected cells, provoking an attack by the innate and adaptive immune systems. It appears that these "induced-self" ligands recognized by the NKG2D receptor may be a precedent for a new strategy of target cell recognition by the immune system.
 CC 15-0 (Immunochemistry)
 ST review NK cell receptor NKG2D MHC
 IT Histocompatibility antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study).
 (MHC (major histocompatibility complex), class I; NK receptors in target cell recognition by NK cells)
 IT Macrophage
 (NK receptors in target cell recognition by NK cells)
 IT TCR .gamma..delta. (receptor)
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (NK receptors in target cell recognition by NK cells)
 IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (NKG2D; NK receptors in target cell recognition by NK cells)

IT Lymphocyte
 (natural killer cell; NK receptors in target cell recognition by NK cells)

REFERENCE COUNT: 150 THERE ARE 150 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:557581 HCAPLUS

DOCUMENT NUMBER: 133:236795

TITLE: Ligands for the murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages

AUTHOR(S): Diefenbach, Andreas; Jamieson, Amanda M.; Liu, Scot D.; Shastri, Nilabh; Raulet, David H.

CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer Research Laboratory, University of California, Berkeley, CA, USA

SOURCE: Nature Immunology (2000), 1(2), 119-126

CODEN: NIAMCZ; ISSN: 1529-2908

PUBLISHER: Nature America Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Natural killer (NK) cells attack tumor and infected cells, but the receptors and ligands that stimulate them are poorly understood. Here we report the expression cloning of two murine ligands for the lectin-like receptor NKG2D. The two ligands, H-60 and Rae-1.beta., are distant relatives of major histocompatibility complex class I mols. NKG2D ligands are not expressed by most normal cells but are up-regulated on numerous tumor cells. We show that mouse NKG2D is expressed by NK cells, activated CD8+T cells and activated macrophages. Expression of either NKG2D ligand by target cells triggers NK cell cytotoxicity and interferon-.gamma. secretion by NK cells, as well as nitric oxide release and tumor necrosis factor .alpha. transcription by macrophages. Thus, through their interaction with NKG2D, H-60 and Rae1.beta. are newly identified potent stimulators of innate immunity.

CC 15-10 (Immunochemistry)

ST NKG2D receptor ligand tumor NK cell macrophage

IT Receptors

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(NKG2D; ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

IT Proteins, specific or class

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(Rae1.beta.; ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

IT Cytotoxicity

Macrophage

Neoplasm

Signal transduction, biological

(ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

IT Tumor necrosis factors

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL

(Biological study); FORM (Formation, nonpreparative)
 (ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

IT Histocompatibility antigens
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (minor, H-60; ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

IT Lymphocyte
 (natural killer cell; ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

IT Interferons
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (.gamma.; ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

IT 10102-43-9, Nitric oxide, biological studies
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (ligands for murine NKG2D receptor: expression by tumor cells and activation of NK cells and macrophages)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 11 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1999:765800 HCPLUS
 DOCUMENT NUMBER: 132:62755
 TITLE: Natural killer cells: stress out, turn on, tune in
 AUTHOR(S): Diefenbach, Andreas; Raulet, David
 H.
 CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer Research Laboratory, University of California at Berkeley, Berkeley, CA, 94720-3200, USA
 SOURCE: Current Biology (1999), 9(22), R851-R853
 CODEN: CUBLE2; ISSN: 0960-9822
 PUBLISHER: Current Biology Publications
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 AB A review with 14 refs. Natural killer cells attack tumor cells, infected cells and some normal cells, but the basis of their specificity is not completely understood. Recent studies indicate that epithelial tumor cells upregulate a stress-induced MHC class-I-like protein termed MICA, triggering NK cells via a recently described receptor called NKG2D.

CC 15-0 (Immunochemistry)
 ST review natural killer cell NKG2D receptor MICA glycoprotein
 IT Glycoproteins, specific or class
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (MICA (MHC class I chain-related-A); MICA ligand/NKG2D receptor interaction in recognition function of natural killer cells)

IT Receptors
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (NKG2D; MICA ligand/NKG2D receptor interaction in recognition function of natural killer cells)

IT Lymphocyte
 (natural killer cell; MICA ligand/NKG2D receptor interaction in recognition function of)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

Harris 09/871,491

22/09/2003

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT